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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/533,981 | 10/05/2005 | Teunis Bernard Geijtenbeek | 294-215 PCT/US | 9614 |

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| EXAMINER | |
|---|---|
| JUEDES, AMY E | |
| ART UNIT | PAPER NUMBER |
| 1644 | |
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| 12/28/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/533,981 | GEIJTENBEEK ET AL. | |
| | Examiner | Art Unit | |
| | AMY E. JUEDES | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *68-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 11/9/09 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/9/09 has been entered.

Claim 68 has been amended.

Claims 68-76 are pending.

2. Upon reconsideration, the species of antigen/disease recited in claims 72-74and 76 are rejoined.

Claims 68-76 are under examination.

3. It is noted that claims 69-71 and 75-76 are incorrectly identified as “new’ claims, when in fact they have been previously presented in the amendment dated 1/29/09.

4. The rejection of the claims under 35 U.S.C. 102 is withdrawn in view of Applicant’s amendment to limit the claims to glycoconjugates comprising a “on-sialylated”Lewis x antigen.

5. The following are new grounds of rejection.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the

specification, while being enabling for:

a method for stimulating an immune response in an individual, and a method of treating autoimmune disease comprising administering an antigen comprising a glyconjugate comprising a non-sialylated Lewis x antigen,

does not reasonably provide enablement for:

a method of treating cancer or a transplantation related disease comprising administering an antigen comprising a glyconjugate comprising a non-sialylated Lewis x antigen.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable claims drawn to the method as broadly claimed. The instant claims are drawn to a method comprising administering an antigen comprising a Lewis x antigen glyconjugate. Antigens

comprising Lewis x glyconjugates are known to be effective at stimulating TH2 immune responses and upregulating Th2 cytokines. However, the instant claim encompasses administering said glyconjugate for the treatment of cancer, autoimmune disease, or transplantation rejection. The ability of a single treatment to be effective for such widely divergent diseases is highly unpredictable. For example, the goal of treating cancer involves stimulating an effective anti-tumor immune response, while the treatment of autoimmune disease usually involves suppressing a pathogenic immune response. Furthermore, glyconjugates comprising Lewis x antigens are know to induce a Th2 response and to impair the function of dendritic cells (see WO 27872 and Nonaka et al., 2008). In fact, the expression of Lewis x antigen by tumor cells is thought to impair the anti-tumor immune response in vivo by inducing the production of Th2 cytokines (see WO 97/27872). Thus, the ability of a glyconjugate comprising said Lewis x antigen to treat cancer would be extremely unpredictable due to its ability to suppress DC function and upregulate Th2 cytokine production. Additionally, the instant claims encompass treatment of a "transplantation-related" disease. This might encompass treating a wide range of divergent conditions, including transplantation rejection, graft versus host disease, or even an allergic reaction to drugs used to suppress rejection. Furthermore, the role of cytokines in transplantation rejection is highly unpredictable, and it is thought that promoting a Th2 response may actually exacerbate the rejection process (see Picotti et al., 1996, page 1956). Thus, it would be extremely unpredictable whether administering a Lewis x glycoconjugate that upregulates Th2 cytokines would be effective for treating transplantation rejection, as is encompassed by the instant claims. Based on the unpredictability of the art, the instant specification must provide a sufficient an enabling disclosure commensurate in scope with the instant claims.

The specification demonstrates the glyconjugates comprising Lewis x bind to DC-SIGN, but does not provide any examples or guidance regarding using a glyconjugate in vivo to induce an immune response sufficient for treating cancer or transplantation related disease. Thus, given the unpredictability of the art, the breadth of the claim, and the lack of guidance provided by the instant specification, it would require undue experimentation to practice the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 68-76 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/27872.

WO 97/27872 teaches a method of stimulating an antigen specific immune response or a Th2 cytokine response comprising administering an antigen comprising a Lewis x antigen glycoconjugate (see page 20, in particular). WO 97/27872 teaches that the method can be performed for the treatment of autoimmune disease (see page 24, in particular). WO 97/27872 teaches that the antigen can comprise a protein, including schistosome egg antigen (an antigen from a parasite), a tumor-associated antigen, or an HIV antigen (a viral antigen, see page 13, in particular). Said proteins inherently comprise peptides capable of binding to MHC class I or II. Additionally, said antigens would inherently bind and be delivered to DC-SIGN, since they comprise the DC-SIGN ligand Lewis x.

Thus, the reference clearly anticipates the invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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